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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,397	02/16/2001	Altaf A. Lal	6395-57049	4907

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,397	LAL ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is responsive to Applicant's response on June 18, 2002. Claims 1, 3-6 and 10 have been amended. Claims 2, 7-9 and 11-12 are cancelled. For clarification purposes, it should be noted that the Rejection of claims 1-3, 5-6 and 10 under 35 U.S.C. 102(b), pages 8-9, paragraph 4 of the previous Office action should have been made under 35 U.S.C. 102(a) in view of Applicant's provisional application (60/097,703) filed August 21,1998. The Office apologizes for this oversight.

2. The Applicant's Declaration filed on June 18, 2002 under 37 CFR 1.131 of Dr. Shi and Exhibits A and B are acknowledged. The Applicant's Declaration filed on June 18, 2002 under 37 CFR 1.131 is sufficient to overcome the Gilbert et al reference.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections/Rejections Withdrawn

4. In view of Applicant's Amendment the following Objections/Rejections are Withdrawn:

a) Objection to claim 10, page 3, paragraph 2 of the previous Office action.
b) Rejection of claims 1-6 and 10 under 35 U.S.C. 112, first paragraph, pages 3-7, paragraph 3 of the Previous Office action.
c) Rejection of claims 1-3, 5-6 and 10 under 102, pages 8-9 of the previous Office action.
d) Rejection of claims 1-3, 5-6 and 10 under 35 U.S.C. 102(a), pages 9-10 of the previous Office action.

New Grounds of Rejection

Claim Objections

5. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claim 3 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 does not further limit claim 1, in fact it broads the scope of independent claim. Claim 1 is directed recombinant peptides that are from two or more stages of the lifecycle of *Plasmodium falciparum*. The lower limit of the claimed invention comprise two peptides each from a different lifecycle of *Plasmodium falciparum*. Claim 3 broads the scope of the claimed invention because SEQ ID NO:2 comprises SEQ ID Nos: 3-25. It is unclear how a recombinant peptide comprising two peptides each from a different lifecycle of *Plasmodium falciparum* can comprise the amino acid sequence of SEQ ID NO:2? Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1,3 5 and 6 are rejected under 35 U.S.C. 102(b) as anticipated by Tine et al *(Infection and Immunity, September 1996, p. 3833-3833).*

Claims 1,3, 5 and 6 are drawn to a recombinant protein comprising peptides from two or more stages in a life cycle of *Plasmodium falciparum* wherein each peptide comprises an antigenic epitope.

Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach [redacted] the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum*

antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1 and 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tine et al *(Infection and Immunity, September 1996, p. 3833-3833)* in view of Schmitt et al *(Molecular Biology Reports Volume 18, 1993, p.223-230).*

Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite

surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column).

Tine et al do not teach the use of a polyhistidine.

Schmitt et al teach affinity purification of histidine-tagged proteins (see the Title). Schmitt et al teach that the expression of recombinant proteins is a standard technique in molecular biology and a wide variety of prokaryotic as well as eukaryotic expression systems are currently in use. Schmitt et al teach that a limiting step is often that the purification of the expressed recombinant protein that yield low expression levels are employed (see the Abstract). Schmitt et al teach that short amino acid sequences can be fused to the recombinant protein as a tag (page 223). Schmitt et al teach that a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow a high expression of purified protein (page 229).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the histidine-tag as taught by Schmitt et al to the recombinant poxvirus vectored multiantigen of Tine et al because Tine et al suggest that a NYVAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). It well known in the art to express, characterize and purify recombinant proteins. It is well known in the art to use signal proteins to express recombinant proteins and to use polyhistidine tags to purify recombinant proteins. Schmitt et al teach a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow purification of the recombinant protein (page 229). It would have been expected barring evidence to the contrary, that the addition of a His-tag to recombinant proteins would allow for high expression of purified protein. The addition of the His-tag is well within the level of skill in the art.

Status of Claims

9. Claim 10 appears to be free of the cited prior art.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
September 26, 2002

LYNETTE R. F. SMITH
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